

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter I of the Patent Cooperation Treaty)

(PCT Rule 44bis)

| | | |
|--|---|---|
| Applicant's or agent's file reference 101062-1 WO | FOR FURTHER ACTION | See item 4 below |
| International application No. PCT/SE2004/000738 | International filing date (<i>day/month/year</i>) 13 May 2004 (13.05.2004) | Priority date (<i>day/month/year</i>) 16 May 2003 (16.05.2003)] |
| International Patent Classification (IPC) or national classification and IPC 7 C07D 235/08, 235/30, A61K 31/502, A61P 29/00 | | |
| Applicant ASTRAZENECA AB | | |

1. This international preliminary report on patentability (Chapter I) is issued by the International Bureau on behalf of the International Searching Authority under Rule 44 bis.1(a).

2. This REPORT consists of a total of 11 sheets, including this cover sheet.

In the attached sheets, any reference to the written opinion of the International Searching Authority should be read as a reference to the international preliminary report on patentability (Chapter I) instead.

3. This report contains indications relating to the following items:

- | | | |
|-------------------------------------|--------------|---|
| <input checked="" type="checkbox"/> | Box No. I | Basis of the report |
| <input checked="" type="checkbox"/> | Box No. II | Priority |
| <input checked="" type="checkbox"/> | Box No. III | Non-establishment of opinion with regard to novelty, inventive step and industrial applicability |
| <input checked="" type="checkbox"/> | Box No. IV | Lack of unity of invention |
| <input checked="" type="checkbox"/> | Box No. V | Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement |
| <input checked="" type="checkbox"/> | Box No. VI | Certain documents cited |
| <input type="checkbox"/> | Box No. VII | Certain defects in the international application |
| <input checked="" type="checkbox"/> | Box No. VIII | Certain observations on the international application |

4. The International Bureau will communicate this report to designated Offices in accordance with Rules 44bis.3(c) and 93bis.1 but not, except where the applicant makes an express request under Article 23(2), before the expiration of 30 months from the priority date (Rule 44bis .2).

| | |
|--|---|
| <p style="text-align: center;">The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland</p> <p>Facsimile No. +41 22 740 14 35</p> | <p>Date of issuance of this report 18 November 2005 (18.11.2005)</p> <p>Authorized officer Philippe Becamel</p> <p>Telephone No. +41 22 338 70 90</p> |
|--|---|

PATENT COOPERATION TREATY

REC'D 16 NOV 2004

WIPO

PCT

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:

Global Intellectual Property
AstraZeneca AB
SE-151 85 Södertälje

Date of mailing
(day/month/year)

11-11-2004

Applicant's or agent's file reference

101062-1 WO

FOR FURTHER ACTION

See paragraph 2 below

International application No.

PCT/SE2004/000738

International filing date (day/month/year)

13.05.2004

Priority date (day/month/year)

16.05.2003

International Patent Classification (IPC) or both national classification and IPC

C07D 235/08, C07D 235/30, A61K 31/502, A61P 29/00,

Applicant

AstraZeneca AB et al

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☒ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further opinions, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/SE

Patent- och registreringsverket

Box 5055

S-102 42 STOCKHOLM

Facsimile No. +46 8 667 72 88

Authorized officer

Fernando Farieta/BS

Telephone No. +46 8 782 25 00

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.

PCT/SE2004/000738

Box No. I **Basis of this opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This opinion has been established on the basis of a translation from the original language into the following language, _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ in written format

☐ in computer readable form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/SE2004/000738

Box No. II Priority

1. ☐ The following document has not yet been furnished:

☐ copy of the earlier application whose priority has been claimed (Rules 43*bis*.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rules 43*bis*.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date is the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43*bis*.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

The priority is considered valid.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/SE2004/000738

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The question whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 18

because:

☒ the said international application, or the said claims Nos. 18
relate to the following subject matter which does not require an international preliminary examination (*specify*):

See PCT Rule 67.1.(iv): Methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods.

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. _____
are so unclear that no meaningful opinion could be formed (*specify*):

☐ The claims, or said claims Nos. _____ are so inadequately supported
by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of
the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not
comply with the technical requirements provided for in the Annex C-bis of the Administrative Instructions.

☐ See Supplemental Box for further details.

WRITTEN OPINION OF THE
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

International application No.

PCT/SE2004/000738

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation (Form PCT/IPEA/206) to pay additional fees the applicant has:
- ☐ paid additional fees
- ☐ paid additional fees under protest
- ☒ Not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ Complied with
- ☐ Not Complied with for the following reasons:

The International Search Authority considers that there are 3 inventions covered by the claims indicated as follows:

I: Claims: 1-18, 21 and part of claims 19-20 directed to benzimidazoles.

II: Part of claims 19-20 directed to phenyl compounds.

III: Claim 22 directed to indol compounds.

The ISA has carried out a partial search which relates to invention I mentioned above.

The present application has been considered to contain III inventions which are not linked such that they form a single general inventive concept, as required by Rules 13.1, 13.2 and 13.3 PCT.

Further the claims 19-20 only seems to comprise use of compounds as intermediates for the compounds of claim 1, several compounds are not considered to be in the scope of formula I of the application.

.../...

4. Consequently, this opinion has been established in respect of the following parts of the international application:
- ☐ all parts
- ☒ the parts relating to claims Nos. 1-18, 21 and partly 19-20

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/SE2004/000738

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box IV

Consequently, the three groups of inventions are not so linked as to form a single general inventive concept as required by Rule 13.1 PCT.

Invention 1 has been searched to the extent it was possible. The novelty search has showed that there are a large number of compounds relevant to the issue of novelty of the present invention and it has not been possible to provide references to all of these compounds. Therefore a limited number of representative compounds have been selected. The selection is based on the compounds which resemble the compounds of claim 8 to the greatest extent and compounds which have a medical use, preferably with the same effect as the claimed compounds.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/SE2004/000738

Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | | |
|-------------------------------|--------|---------------------------|-----|
| Novelty (N) | Claims | 1-18, 21 and partly 19-20 | YES |
| | Claims | | NO |
| Inventive step (IS) | Claims | | YES |
| | Claims | 1-18, 21 and partly 19-20 | NO |
| Industrial applicability (IA) | Claims | 1-18, 21 and partly 19-20 | YES |
| | Claims | | NO |

2. Citations and explanations:

The following documents have been found to be relevant:

D1: EP0419210 A1

Novel benzimidazole compounds and their use as antiallergy and anti-inflammatory agents.

D2: WO 01/96336 A2

6, 5 - fused bicyclic heterocycles useful for diseases involving chemotaxis and monocytes.

D3: " Cyanoethylation of benzimidazoles" Vol 24B, (1985) pp 1098-1101. Indian Journal of Chemistry.

The benzimidazoles pharmacological activities had been determined. (scheme 1 table 1).

The problem the present invention aims to solve is to provide compounds useful in the treatment of pain and disorders mediated by VR1.

The cited document represents the general state of the art. The invention defined in claims 1-18, 21 and partly 19-20 is not disclosed by this document. No compound with a substituent R2 in position 7 has been found according to the claimed formula I. The claims 1-18, 21 and partly 19-20 are considered to fulfil the requirements of novelty.

.../...

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/SE2004/000738

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box V

The compounds of claims 1-18, 21 and partly 19-20 are structurally very similar to these compounds. The compounds of formula (I) are through D1-D2 and even D3 known to be useful in the treatment of pain/inflammation and certain disorders named in the application (claim 13-15). It is considered to be obvious to a person skilled in the art to use also the compounds of claim 19 to treat these disorders. The invention according to claims 1-18, 21 and partly 19-20 is considered to lack inventive step and is not patentable.

Such a selection can only be regarded as inventive, if the novel benzimidazol compounds present unexpected effects or properties in relation to the rest of the documents D1-D3. However, no such effects or properties are indicated in the application. Hence, no inventive step is present in the subject-matter of claims 1-18, 21 and partly 19-20.

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.
PCT/SE2004/000738

Box No. VI Certain documents cited

1. Certain published documents (Rules 43bis.1 and 70.10)

| | <u>Application No. Patent No.</u> | <u>Publication date (day/month/year)</u> | <u>Filing date (day/month/year)</u> | <u>Priority date (valid claim) (day/month/year)</u> |
|------|---------------------------------------|--|---|---|
| P, X | WO2004/000828 | 31.12.03 | 19.06.03 | 20.06.02 |

2. Non-written disclosures (Rules 43bis.1 and 70.9)

| <u>Kind of non-written disclosure</u> | <u>Date of non-written disclosure (day/month/year)</u> | <u>Date of written disclosure referring to non-written disclosure (day/month/year)</u> |
|---------------------------------------|--|--|
|---------------------------------------|--|--|

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY

International application No.

PCT/SE2004/000738

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawing or on the question whether the claim are fully supported by the description, are made:

Claims 10 and 12

The expression "VR1 mediated disorders" is not considered to be clear as it defines the intended disorders with reference to the underlying mechanism instead of specifying the actual disorders. Claims 10 and 12 do not fulfil the demands of clarity of 8 § PL. The search and the opinion are based on the disorders and conditions named in claims 13-15.

Claim 19

It should be pointed out that claim 19 is considered to be unclear as it does not say what compounds are intended as product only that they should be suitable for the treatment of VR1 mediated disorders. Further the claim only seems to comprise use of compounds as intermediates for the compounds of claim 1 that seems obvious to a person skilled in the art and the compounds themselves are probably known.